REMARKS/ARGUMENTS

Claims 4, 5, 10-13, and 15-16 are pending in the application. Claim 15 was amended herein to remove an exemplary phrase. Claim 16 has been added. Reconsideration of the claims in view of the following Remarks is respectfully requested.

Double Patenting Rejection

Claims 4, 5, 10-13, and 15 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-5, and 9-13 of copending Application No. 09/838,821.

Upon notice of allowable claims, Applicant will file a terminal disclaimer in compliance with 37 C.F.R. 1.321(c) as appropriate to overcome this rejection.

35 U.S.C. § 103(a) Rejection

Claims 4, 5, 10-13, and 15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Myers et al. The Examiner contends that Myers et al. teaches a quinazoline compound as claimed in a method to treat cell signaling, cell proliferation, cell inflammatory response, and useful protein tyrosine kinase (PTK) inhibitors and activity. The Examiner further asserts that it would be obvious to modify Myers et al. to obtain Applicant's invention.

The Applicant respectfully traverses this rejection. Applicants submit that the Examiner has not established a *prima facie* case of obviousness at least because the reference does not disclose all of the elements of the claimed invention, and because there is no motivation provided in the reference to modify its teachings to obtain Applicant's claimed invention. Applicant's claims are directed to a method for specifically inhibiting c-jun activation in mammalian or avian cells comprising contacting the cells with an effective inhibitory amount of a compound of formula (I). In the course of studying radiation-induced c-jun activation, the Applicant unexpectedly discovered that an inhibitor of Janus family kinase 3 (JAK-3) abrogated radiation-induced c-jun activation (page 8-9 of the specification; Example 1, pages 21-25). The Applicant further discovered that inhibition of other tyrosine kinases, including BTK, SYK, or LYN, failed to inhibit c-jun expression.

The Applicant submits that nowhere does Myers et al. disclose or suggest the use of a compound of formula (I) to specifically inhibit c-jun activation. Rather, this reference discloses various quinazoline compounds that inhibit EGF and/or PDGF receptor tyrosine kinases. The reference fails to provide any association between c-jun activation and the inhibition of any *particular* protein kinase. Myers et al. does not teach or suggest that *specific* inhibition of c-jun is achievable through inhibition of JAK-3. Nor does Myers et al. disclose or suggest that the quinazoline compounds of the invention can specifically inhibit c-jun activation.

Furthermore, Myers et al. does not provide any suggestion that it would be desirable to specifically inhibit c-jun activation as opposed to any other downstream component in the signaling pathway. Therefore, not only does Myers et al. not disclose all elements of the invention as claimed, the reference does not provide any motivation to modify the methods of the reference to obtain a method for specifically inhibiting c-jun using a compound of formula (I). Therefore, Applicant submits that claims 4, 5, 10-13, and 15 are patentable over Myers et al. Withdrawal of the rejection is respectfully requested.

Claims 4, 5, 10-13, and 15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Ihle et al. in view of Narla et al. and Chae et al. The Examiner contends that it would be obvious to arrive at the invention because Ihle et al. allegedly teaches a method to inhibit JAK-3, Narla et al. teaches an inhibitor of PTK, and Chae teaches that ionizing radiation results in the activation of c-jun.

The Applicant respectfully traverses this rejection. In order to establish a *prima facie* case of obviousness, the Examiner must show a) that the references disclose all of the elements of the invention, b) that there would be motivation to combine the references to modify the teaching of the reference to obtain Applicant's claimed invention, and c) a reasonable expectation of success. The Applicant submits that the Examiner has not established even a *prima facie* case of obviousness at least because the references do not disclose all of the elements of the claimed invention, and there is no motivation provided in the references to modify the teachings of the cited references to obtain Applicant's claimed invention.

Applicant's claims are directed to a method for specifically inhibiting c-jun activation in mammalian or avian cells comprising contacting the cells with an effective inhibitory amount of a compound of formula (I). Ihle et al. discloses methods for regulating cellular responses to cytokines by inhibiting or enhancing at least one Jak kinase activity that mediates the response.

Ihle et al., however, does not teach or suggest specifically inhibiting c-jun activation. Furthermore, Ihle et al. does not disclose or suggest that specifically inhibiting c-jun activation, as recited in the present claims, is desirable. Nor does this reference teach or suggest that inhibiting JAK-3 kinase activity, as opposed to any other kinase activity, will result in specific inhibition of c-jun activation. Ihle also does not even suggest compounds of Formula I regulating cellular responses to cytokines by inhibiting or enhancing at least one Jak kinase activity that mediates the response.

The addition of the Narla et al. and Chae et al. references does not remedy the deficiencies of Ihle et al. Chae et al. discloses that protein tyrosine kinase activation precedes and perhaps mandates radiation-induced activation of c-jun protooncogene expression in human lymphohematopoietic precursors. Chae et al. does not, however, teach or suggest that c-jun expression can be specifically inhibited through inhibition of JAK-3 kinase activity. Chae et al. also does not describe or suggest quinazoline compounds.

Narla et al. teaches a quinazoline derivative as an inhibitor of the EGF-R tyrosine kinase. Narla et al., however, does not teach or suggest that the quinazoline derivative can specifically inhibit c-jun activation, or that it would be desirable to do so.

Since neither Ihle et al., Narla et al., nor Chae et al. teach or suggest specifically inhibiting c-jun activation, Applicant submits that the cited references, alone or in combination, do not teach all the elements of the present claims. Claims 4, 5, 10-13, and 15, therefore, are patentable over these references.

The Applicant also submits that there is no motivation provided in the references to combine them in order to obtain the claimed invention. To establish obviousness, there must be some teaching, suggestion, or motivation to do so provided in the references themselves. MPEP § 2143.01. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. MPEP 2143 (citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

The Examiner contends that Ihle et al. teaches using a protein to inhibit the activity of JAK-3, and that such an inhibitor will have the effect of inhibiting c-jun activation. Narla et al. is asserted to teach a quinazoline derivative as an inhibitor of the EGF-R tyrosine kinase. Chae et al. is asserted to teach that protein tyrosine kinase activation precedes c-jun protooncogene expression. The Examiner then apparently concludes there is motivation to substitute the

inhibitors of Ihle et al. with the quinazoline derivative of Narla et al. Neither Ihle et al., Narla et al., nor Chae et al., however, disclose that the quinazoline derivative of Narla et al. would inhibit JAK-3 as taught by Ihle et al. Therefore, one of ordinary skill in the art would find no motivation to substitute the quinazoline derivatives taught by Narla et al. for the inhibitors taught by Ihle et al. to inhibit JAK-3, thereby specifically inhibiting c-jun activation, as recited by the present claims.

Applicant submits that it is the instant specification that discloses that quinazoline compounds such as those disclosed in Narla et al. can specifically inhibit c-jun expression and JAK-3. The Examiner, therefore, is improperly using the unexpected discoveries of the instant specification to supply the motivation to combine the Narla et al. and Ihle et al. references. Therefore, claims 4, 5, 10-13, and 15 are patentable over the cited references for at least this additional reason.

Summary

Applicant submits that the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicant's representative if prosecution may be advanced thereby.

Respectfully submitted,

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Date: September 18, 2003

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